We Claim:

1. A method for making a laspartomycin core peptide, salt or hydrate thereof, comprising the steps of:

culturing the microorganism *Streptomyces viridochromogenes,* ssp. *komabensis* (ATCC 29814) in a culture medium;

isolating laspartomycin from the culture medium; and

cleaving a lipophilic fragment from laspartomycin, thereby yielding the laspartomycin core peptide.

2. The method of Claim 1 further including the step of isolating the laspartomycin core peptide.

3. The method of Claim 1 in which the culturing step is carried out at a temperature in the range of about 24°C to about 34°C.

4. The method of Claim 3 in which the temperature is in the range of about 27°C to about 29°C.

5. The method of Claim 1 in which the microorganism is removed from the culture medium prior to isolating laspartomycin.

6. The method of Claim 5 in which the culture medium is acidified prior to removing the microorganism.

7. The method of Claim 6 in which the culture medium is acidified to a pH in the range of about 2.0 to about 3.0.

8. The method of Claim 7 in which the microorganism is removed *via* centrifugation and suspended in water, thereby providing an aqueous suspension.

9. The method of Claim 8 in which the pH of the aqueous suspension is adjusted to a basic pH.

10. The method of Claim 8 in which a divalent cation concentration of the aqueous suspension is adjusted to between about 4mmol/l to about 10 mmol/l and the pH of the aqueous suspension is adjusted to a basic pH.

11. The method of Claim 9 or 10 in which the adjusted pH is in the range of about pH 8.0 to about pH 9.0.

12. The method of Claim 10 in which the divalent cation is selected from the group consisting of Ca^{2+}, Mg^{2+} and Zn^{+2}.

13. The method of either of Claim 9 or Claim 10, in which laspartomycin is extracted into organic solvent, thereby providing an organic solvent extract of laspartomycin.

14. The method of Claim 13 further comprising:

acidifying the organic solvent extract of laspartomycin;
extracting laspartomycin into aqueous solution;
extracting laspartomycin into organic solvent;
extracting laspartomycin into aqueous solution; and
concentrating the aqueous solution to provide a salt of laspartomycin.

15. The method of Claim 14 in which the organic solvent is 1-butanol.

16. The method of Claim 14, wherein the salt of laspartomycin is extracted into aqueous solution by washing the organic solvent extract of laspartomycin with aqueous base solution.

17. The method of Claim 14, wherein laspartomycin is extracted into organic solvent by acidifying the aqueous solution of the salt of laspartomycin.

18. The method of Claim 14, further comprising:

dissolving the salt of laspartomycin in aqueous acid solution;

extracting laspartomycin into organic solvent; and

removing the organic solvent to provide laspartomycin.

19. The method of Claim 1 in which the lipophilic fragment is cleaved with an enzyme.

20. The method of Claim 19 in which the enzyme is a deacylase.

21. The method of Claim 1 in which the cleavage step further comprises:

culturing a microorganism capable of producing a deacylase in a culture medium; and

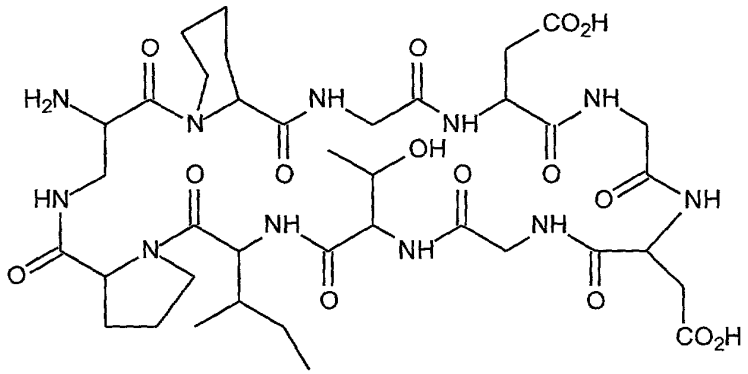
contacting laspartomycin with the culture medium.

22. The method of Claim 21 in which the microorganism is *Actinoplanes utahensis* (NRRL 12052).

23. The method of Claim 22 in which laspartomycin is contacted with the culture medium for about 16 hours at about 29°C.

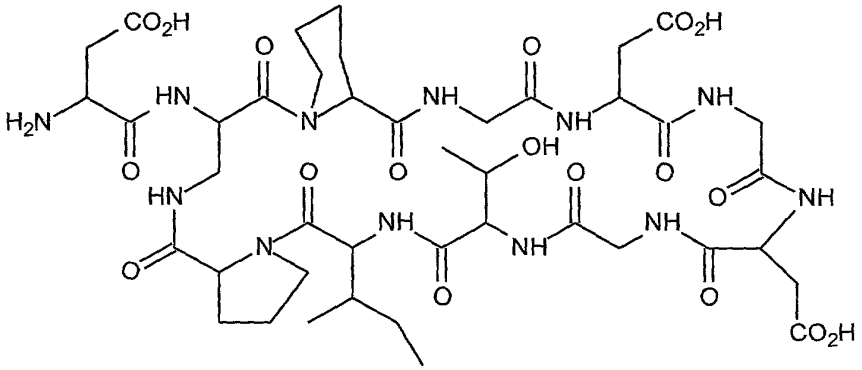
24. The method of Claim 22 in which laspartomycin is contacted with the culture medium for about 4 hours at about 29°C.

25. The method of Claim 23 in which the laspartomycin core peptide has the structure:



or a salt or hydrate thereof.

26. The method of Claim 24 in which the laspartomycin core peptide has the structure:



or a salt or hydrate thereof.

27. The laspartomycin core peptide produced by the method of any one of Claims 1, 23 and 24.

28. A laspartomycin core peptide derivative according to structural formula (I):

(I) $Y^1—L—X^1—N(R^1)—R$

or a salt or hydrate thereof, wherein either:

(i) Y^1—L—X^1 taken together is hydrogen; or

(ii) Y^1 is a linking group;

L is a linker;

X^1 is selected from the group consisting of —CO—, —SO_2—, —CS—, —PO—, —OPO—,—OC(O)—, —NHCO— and —NR^1CO—;

N is nitrogen;

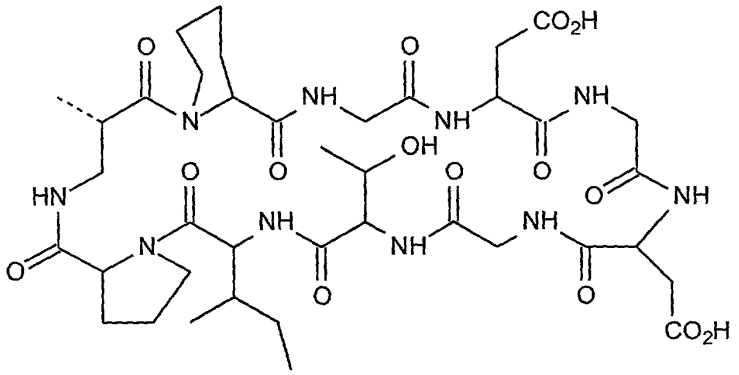
R^1 is selected from the group consisting of hydrogen, (C_1-C_{10}) alkyl optionally substituted with one or more of the same or different R^2 groups, (C_1-C_{10}) heteroalkyl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{10}) aryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{15}) arylaryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{15}) biaryl optionally substituted with one or more of the same or different R^2 groups, five to ten membered heteroaryl optionally substituted with one or more of the same or different R^2 groups, (C_6-C_{16}) arylalkyl optionally substituted with one or more of the same or different R^2 groups and six to sixteen membered heteroarylalkyl optionally substituted with one or more of the same or different R^2 groups;

each R^2 is independently selected from the group consisting of —OR^3, —SR^3, —NR^3R^3, —CN, —NO_2, —N_3, —C(O)OR^3, —C(O)NR^3R^3, —C(S)NR^3R^3, -C(NR^3)NR^3R^3, —CHO, —R^3CO, —SO_2R^3, —SOR^3, —$PO(OR^3)_2$, —$PO(OR^3)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

each R^3 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, 5-10 membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

R is the core cyclic peptide of laspartomycin.

29. The laspartomycin core peptide derivative of Claim 28 wherein R has the structure:

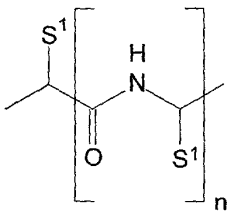


30. The laspartomycin core peptide derivative of Claim 29 in which Y^1 is selected from the group consisting of —NHR^1, —NH_2, —OH, —SH, —PH, halogen, —CHO, —R^1CO, —SO_2H, —PO_2H, —N_3, —CN, —CO_2H, —SO_3H, —PO_3H, —$PO_2(OR^1)H$, —CO_2R^1, —SO_3R^1, and —$PO(OR^1)_2$.

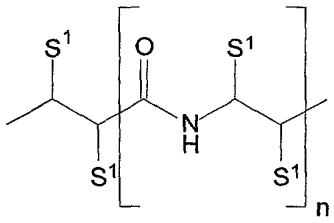
31. The laspartomycin core peptide derivative of Claim 30 in which R^1 is hydrogen.

32. The laspartomycin core peptide derivative of Claim 31 in which Y^1 is selected from the group consisting of —SH, H_2N—, —OH, —CO_2H and —CO_2R, X^1 is carbonyl and L is selected from the group consisting of:

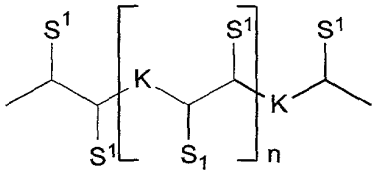
(L1)



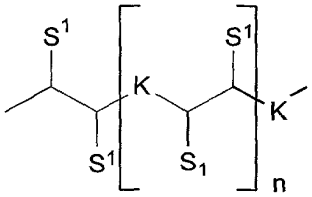
(L2)



(L3)



(L4)



or a salt or hydrate thereof, wherein:

n is 0, 1, 2 or 3;

each S^1 is selected from the group consisting of hydrogen, (C_1-C_{10}) alkyl optionally substituted with one or more of the same or different R^4 groups, (C_1-C_{10}) heteroalkyl optionally substituted with one or more of the same or different R^4 groups, (C_5-C_{10}) aryl optionally substituted with one or more of the same or different R^4 groups, (C_5-C_{15}) arylaryl optionally substituted with one or more of the same or different R^4 groups, (C_5-C_{15}) biaryl optionally substituted with one or more of the same or different R^4 groups, five to ten membered heteroaryl optionally substituted with one or more of the same or different R^4 groups, (C_6-C_{16}) arylalkyl optionally substituted with one or more of the same or different R^4 groups and six to sixteen membered heteroarylalkyl optionally substituted with one or more of the same or different R^4 groups;

each R^4 is independently selected from the group consisting of —OR^5, —SR^5, —NR^5R^5, —CN, —NO_2, —N_3, —$C(O)OR^5$, —$C(O)NR^5R^5$, —$C(S)NR^5R^5$, —$C(NR^5)NR^5R^5$, —CHO, —R^5CO, —SO_2R^5, —SOR^5, —$PO(OR^5)_2$, —$PO(OR^5)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

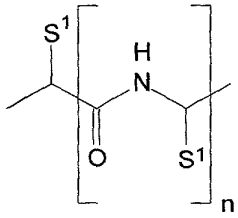
each R^5 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, 5-10 membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

each K is independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

33. The laspartomycin core peptide derivative of Claim 32 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

34. The laspartomycin core peptide derivative of Claim 32 in which Y^1 is H_2N— and L is:

L1



35. The laspartomycin core peptide derivative of Claim 34 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

36. The laspartomycin core peptide derivative of Claim 35 in which n is 0 and S^1 is $-CH_2C(O)OH$ or a salt or hydrate thereof.

37. The laspartomycin core peptide derivative of Claim 35 in which n is 1 and S^1 is $-CH_2CO_2H$ or a salt or hydrate thereof and S^2 is $-CH_2$–indol-2-yl.

38. The laspartomycin core peptide derivative of Claim 28 in which Y^1—L—X^1 taken together is hydrogen and R^1 is hydrogen.

39. A method for making a laspartomycin core peptide derivative comprising covalently attaching a linker moiety to a laspartomycin core peptide.

40. A method of making a antimicrobial laspartomycin derivative comprising:

covalently attaching a linker moiety to a laspartomycin core peptide, thereby providing a laspartomycin core peptide derivative; and

covalently attaching a lipophilic group to the laspartomycin core peptide derivative to yield a antimicrobial laspartomycin derivative.

41. The method of Claim 40 further including the step of isolating the antimicrobial laspartomycin derivative.

42. The method of Claim 40 in which the laspartomycin core peptide is provided by the method of any one of Claims 1, 23 and 24.

43. The method of Claim 40 in which the laspartomycin core peptide is a compound according to any one of Claims 36 and 38.

44. A method of making a antimicrobial laspartomycin derivative comprising:

covalently attaching a lipophilic group to a linker, thereby providing a lipophilic-linker group; and

covalently attaching the lipophilic-linker group to the laspartomycin core peptide derivative thereby yielding a antimicrobial laspartomycin derivative.

45. The method of Claim 44 further including the step of isolating the antimicrobial laspartomycin derivative.

46. The method of Claim 44 in which the laspartomycin core peptide is provided by the method of any one of Claims 1, 23 and 24.

47. The method of Claim 44 in which the laspartomycin core peptide is a compound according to any one of Claims 36 and 38.

48. The laspartomycin derivative provided by the method of any one of Claims 40 and 44.

49. An isolated antimicrobial laspartomycin derivative according to structural formula (II):

(II) $Y^2—(X^2—X^3)—L—X^1—N(R^1)—R$

or an pharmaceutically acceptable salt or hydrate thereof, wherein:

Y^2 is a lipophilic group;

X^1 is selected from the group consisting of —CO—, —SO_2—, —CS—, —PO—, —OPO—,—OC(O)—, —NHCO— and —NR^1CO—;

X^2 is a linked group;

X^3 is a linked group;

L is a linker;

N is nitrogen;

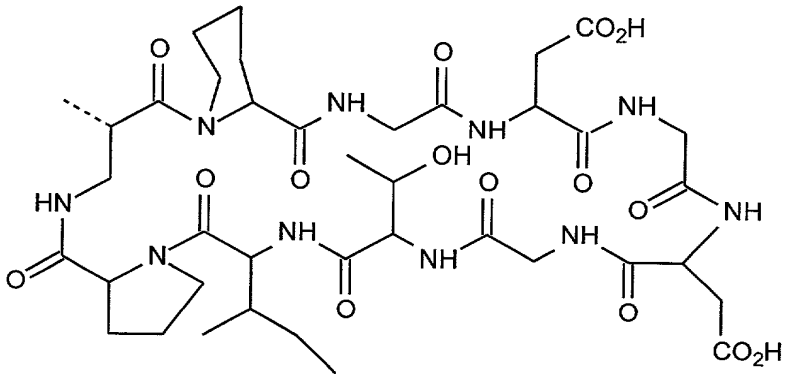
R^1 is selected from the group consisting of hydrogen, (C_1-C_{10}) alkyl optionally substituted with one or more of the same or different R^2 groups, (C_1-C_{10}) heteroalkyl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{10}) aryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{15}) arylaryl optionally substituted with one or more of the same or different R^2 groups, (C_5-C_{15}) biaryl optionally substituted with one or more of the same or different R^2 groups, five to ten membered heteroaryl optionally substituted with one or more of the same or different R^2 groups, (C_6-C_{16}) arylalkyl optionally substituted with one or more of the same or different R^2 groups and six to sixteen membered heteroarylalkyl optionally substituted with one or more of the same or different R^2 groups;

each R^2 is independently selected from the group consisting of —OR^3, —SR^3, —NR^3R^3, —CN, —NO_2, —N_3, —$C(O)OR^3$, —$C(O)NR^3R^3$, —$C(S)NR^3R^3$, -$C(NR^3)NR^3R^3$, —CHO, —R^3CO, —SO_2R^3, —SOR^3, —$PO(OR^3)_2$, —$PO(OR^3)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

each R^3 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, 5-10 membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

R is the core cyclic peptide of laspartomycin.

50. The laspartomycin derivative Claim 49 in which R has the structure:

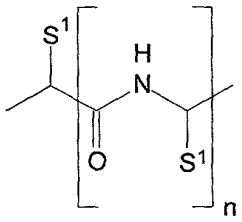


51. The laspartomycin derivative of Claim 50 in which (X^2—X^3) taken together are selected from the group consisting of —C(O)O—, —O(O)C—, —CONH—, —NHCO—, —CONR^1—, —NR^{1}CO—,—C(O)S—, —S(O)C—, —OSO$_2$—, —S(O$_2$)O—, —NHSO$_2$—, —NR^{1}SO$_2$, —S(O$_2$)NH—, —S(O$_2$)NR^1—, C(S)NH—,—NHC(S)—, —NHP(O)—, —P(O)NH—, —OP(O)—, —P(O)O—, —SP(O)—, —P(O)S—, —OC(O)NH—, —NHC(O)O—, —OC(O)NR^1—, —NR^{1}C(O)O—, —OC(O)O—, —NHC(O)NH—, —NHC(O)NR^1—, —NR^{1}C(O)NH— and NR^{1}C(O)NR^1.

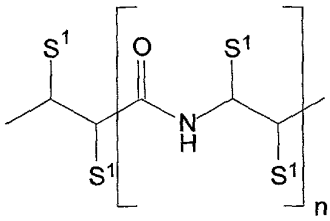
52. The laspartomycin derivative of Claim 51 in which R^1 is hydrogen.

53. The laspartomycin derivative of Claim 52 in which X^1 is —CO— or—SO$_2$—, and L is selected from the group consisting of:

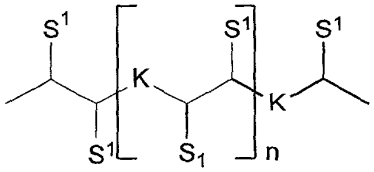
(L1)



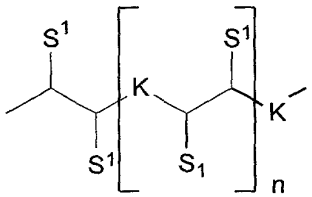
(L2)



(L3)



(L4)



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is 0, 1, 2 or 3;

each S^1 is selected from the group consisting of hydrogen, (C_1-C_{10}) alkyl optionally substituted with one or more of the same or different R^4 groups, (C_1-C_{10}) heteroalkyl optionally substituted with one or more of the same or different R^4 groups, (C_5-C_{10}) aryl optionally substituted with one or more of the same or different R^4 groups, (C_5-C_{15}) arylaryl optionally substituted with one or more of the same or different R^4 groups,(C_5-C_{15}) biaryl optionally substituted with one or more of the same or different R^4 groups, five to ten membered heteroaryl optionally substituted with one or more of the same or different R^4 groups, (C_6-C_{16}) arylalkyl optionally substituted with one or more of the same or different R^4 groups and six to sixteen membered heteroarylalkyl optionally substituted with one or more of the same or different R^4 groups;

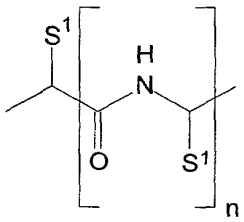
each R^4 is independently selected from the group consisting of —OR^5, —SR^5, —NR^5R^5, —CN, —NO_2, —N_3, —$C(O)OR^5$, —$C(O)NR^5R^5$, —$C(S)NR^5R^5$, —$C(NR^5)NR^5R^5$, —CHO, —R^5CO, —SO_2R^5, —SOR^5, —$PO(OR^5)_2$, —$PO(OR^5)$, —CO_2H, —SO_3H, —PO_3H, halogen and trihalomethyl;

each R^5 is independently selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_5-C_{10}) aryl, 5-10 membered heteroaryl, (C_6-C_{16}) arylalkyl and six to sixteen membered heteroarylalkyl; and

each K is independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

54. The compound of Claim 53 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

55. The compound of Claim 53 in which L is:



56. The laspartomycin derivative of Claim 55 in which each S^1 is independently a side-chain of a genetically encoded α-amino acid.

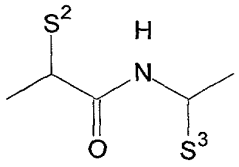
57. The laspartomycin derivative of Claim 55 in which n is 0.

58. The laspartomycin derivative of Claim 57 in which S^1 is $–CH_2–CO_2H$ or a pharmaceutically acceptable salt or hydrate thereof.

59. The laspartomycin derivative of Claim 58 in which (X^2—X^3) taken together are —CONH—.

60. The laspartomycin derivative of Claim 59 in which Y^2 is tetradecan-1-yl.

61. The laspartomycin derivative of Claim 55 in which L is:



or a salt or hydrate thereof, wherein S^2 and S^3 are each independently a side chain of a genetically encoded α-amino acid.

62. The laspartomycin derivative of Claim 61 in which S^2 is $-CH_2-$indol-2-yl and S^3 is $-CH_2-CO_2H$ or a pharmaceutically acceptable salt or hydrate thereof.

63. The laspartomycin derivative of Claim 62 in which (X^2—X^3) taken together are —CONH—.

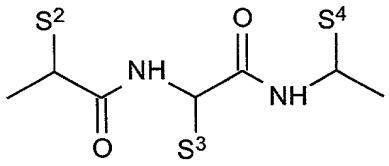
64. The laspartomycin derivative of Claim 63 in which Y^2 is nonan-1-yl.

65. The laspartomycin derivative of Claim 61 in which S^2 is hydrogen and S^3 is $-CH_2-CO_2H$ or a salt thereof.

66. The laspartomycin derivative of Claim 65 in which (X^2—X^3) taken together are $—SO_2NH—$.

67. The laspartomycin derivative of Claim 66 in which Y^2 is decan-1-yl.

68. The laspartomycin derivative of Claim 55 in which L is:



or a salt or hydrate thereof, wherein S^2, S^3 and S^4 are each independently a side chain of a genetically encoded α-amino acid.

69. The laspartomycin derivative of Claim 68 in which S^2 is $-CH_2-$indol-2-yl, S^3 is $-CH_2-CO_2H$ or a salt thereof and S^4 is $-CH_2-CO_2H$ or a salt thereof.

70. The laspartomycin derivative of Claim 69 in which (X^2—X^3) taken together are —CONH—.

71. The laspartomycin derivative of Claim 70 in which Y^2 is nonan-1-yl.

72. A pharmaceutical composition comprising a compound according to Claim 48 and a pharmaceutically acceptable excipient, carrier or diluent.

73. A method for treating a microbial infection, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 49.

74. A method for treating a microbial infection, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 71 .

75. A method of inhibiting microbial growth, said method comprising the step of administering to a microbe an effective amount of a compound according to Claim 48.

76. A pharmaceutical composition comprising a compound according to Claim 49 and a pharmaceutically acceptable excipient, carrier or diluent.

77. A method for treating a microbial infection, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 49.

78. A method for treating a microbial infection, said method comprising the step of administering to a subject an effective amount of a compound according to Claim 75.

79. A method of inhibiting microbial growth, said method comprising the step of administering to a microbe an effective amount of a compound according to Claim 49.